

BIOGRAPHICAL SKETCH

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|--|---|-------------|----------------|
| NAME Hollenbach, Andrew Durrell | POSITION TITLE Associate Professor of Genetics | | |
| eRA COMMONS USER NAME aholle | | | |
| EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing,</i> | | | |
| INSTITUTION AND LOCATION | DEGREE (if applicable) | YEAR(s) | FIELD OF STUDY |
| University of Delaware, Newark, DE | B.S. (cum laude) | 1985 – 1989 | Chemistry |
| Johns Hopkins University, Baltimore, MD | Ph.D. | 1989 – 1995 | Biochemistry |
| St. Jude Children's Research Hospital, Memphis, TN | Post-doctoral Researcher | 1995 – 2001 | Genetics |

A. PERSONAL STATEMENT:

I am a National Cancer Institute funded researcher and I will serve as the sole Principal Investigator of this project. I performed my postdoctoral research in the laboratory of Dr. Gerard Grosveld at St. Jude Children's Research Hospital (Memphis, TN) where my studies focused on understanding the regulation of the myogenic transcription factor Pax3 and how the oncogenic fusion protein Pax3-FOXO1 alters normal activity to contribute to the development of the childhood solid muscle tumor Alveolar Rhabdomyosarcoma (ARMS). My present work as an independent, published and funded investigator is a continuation of this work focusing more specifically on how phosphorylation of Pax3 and Pax3-FOXO1 contribute to the regulation of the expression of genes important for muscle differentiation and ARMS tumor development, respectively. The project described in this application developed directly from these earlier investigations resulting from data obtained and published from my lab. These results, ***combined with the extensive similarities of the biological role Pax3 plays in myogenesis and melanoma development***, prompted me to initiate investigations into understanding the role that Pax3 phosphorylation plays in the development of melanoma. However, despite my extensive experience working with Pax3, ***my lack of publication in the field of melanoma research prevents me from successfully obtaining federal extramural funding. Therefore, the present application will provide me funds to obtain solid preliminary data that will allow me to publish in the field of melanoma research thereby establishing my work in the field and situating me suitably for submission of a grant to the National Cancer Institute on an R01 level.*** Of particular importance to the feasibility of this proposal is my extensive experience in studying Pax3 biological activities and in the use of the techniques and theories required to analyze gene expression and transcriptional activity, including DNA binding, transcriptional reporter assays, real time RT-PCR, co-immunoprecipitation and interaction studies, and mutational analysis, as evidenced by my publication record. I have published many peer-reviewed articles in the field of Pax3. I am a member of the Louisiana Cancer Research Consortium (LCRC) at Louisiana State University Health Sciences Center. Through the LCRC I will have access to resources and faculty who are experts in the field of cancer and melanoma research. Finally, my administrative experience as the PI of federally-funded (NCI – R01CA138656), Louisiana state-funded (Board of Regents #067A-04), and institutional-funded grants, in addition to my over eight years of experience managing projects within the lab, attest to my ability to meet the administrative needs of the proposed project.

B. POSITIONS AND HONORS:

Positions and Employment

1989 – 1995 Graduate Researcher, Johns Hopkins University, Baltimore, MD
1995 – 2001 Postdoctoral Researcher, St. Jude Children's Research Hospital, Memphis, TN

2001 – 2003 Research Associate in Genetics, St. Jude Children's Research Hospital, Memphis, TN
2003 – 2010 Assistant Professor of Genetics, Louisiana State University Health Sciences Center, New Orleans, LA
2010 – present Associate Professor of Genetics, Louisiana State University Health Sciences Center, New Orleans, LA

Other Experience and Professional Memberships:

1998 – 1999 Member, St. Jude Children's Research Hospital Postdoctoral Review Committee
1998 – 2001 Member, Executive Council for the St. Jude Children's Research Hospital Council of Postdoctoral Fellows
2001 – 2003 Member, St. Jude Children's Research Hospital Institutional Animal Care and Usage Committee
2006 – 2008 The American Society for Human Genetics
2009 – present The American Society for Biochemistry and Molecular Biology
2010 Reviewer, Florida Department of Health James & Esther King Biomedical Research/Bankhead-Coley Cancer Research Program grants
2010 Reviewer, Italian Ministry of Health Young Research Grants
2011 Reviewer, Swiss National Science Foundation
2011 (March) Reviewer, National Institutes of Health, Interdisciplinary Molecular Sciences and Training Review Panel, F09 Study Section on Oncological Sciences
2011 (July) Reviewer, National Institutes of Health, Interdisciplinary Molecular Sciences and Training Review Panel, F08 Study Section on Genes, Genomes, and Genetics
2011 (October) Reviewer, National Institutes of Health, Interdisciplinary Molecular Sciences and Training Review Panel, F08 Study Section on Genes, Genomes, and Genetics
Ad hoc reviewer Carcinogenesis, BMC Biotechnology, Experimental Cell Research, International Journal of Biochemistry and Cell Biology, Journal of Biomedicine and Biotechnology, Journal of Molecular Biology, Molecular and Cellular Biology, Nucleic Acids Research, Protein Expression and Purification
Member Editorial Board, ISRN Molecular Biology

Honors:

1993 The Harry D. Kruse Award in Nutrition and Public Health, The Johns Hopkins University School of Hygiene and Public Health, Baltimore, MD
2006 Louisiana Cancer Research Consortium Immediate Response Award, Louisiana State University Health Sciences Center, New Orleans, LA
2008 Louisiana Cancer Research Consortium Travel Award, Louisiana State University Health Sciences Center, New Orleans, LA

C. SELECTED PEER-REVIEWED PUBLICATIONS:

Most relevant to the current application (in chronological order):

1. Lam, P. Y.-P., Sublett, J. E., **Hollenbach, A. D.** and Roussel, M. F. (1999) "The oncogenic potential of the Pax3-FKHR fusion protein requires the Pax3 homeodomain recognition helix but not the Pax3 paired-box DNA binding domain." *Mol. Cell. Biol.* 19, 594-601. (PMCID: PMC83917)
2. **Hollenbach, A. D.**, Sublett, J. E., McPherson, C. J. and Grosveld, G. (1999) "The Pax3-FKHR oncoprotein is unresponsive to the Pax3-associated repressor hDaxx." *EMBO Journal* 18, 3702-3711. (PMCID: PMC1171447)
3. **Hollenbach, A. D.**, McPherson, C. J., Lagutina, I., and Grosveld, G. (2002) "The EF-hand calcium-binding protein calmyrin inhibits the DNA-binding and transcriptional activity of Pax3." *Biochim. Biophys. Acta* 1574(3), 321-328. (PMID: 11997098)
4. Pritchard, C., Grosveld G. and **Hollenbach, A. D.** (2003) "Alternative splicing of Pax3 produces a transcriptionally inactive protein." *Gene* 305, 61-69. (PMID: 12594042)
5. Miller, P. J. and **Hollenbach, A. D.** (2007) "The oncogenic fusion protein Pax3-FKHR has a greater post-translational stability relative to Pax3 during early myogenesis" *Biochim. Biophys. Acta* 1770(10), 1450 – 1458. (PMCID: PMC2043499)

6. Miller, P. J.*, Dietz, K. N.*, and **Hollenbach, A. D.** (2008) "Identification of serine 205 as a site of phosphorylation on Pax3 in proliferating but not differentiating primary myoblasts" *Protein Sci* 17:1979-86. (PMCID: PMC2578802)
7. Dietz, K. N., Miller P. J., and **Hollenbach, A. D.** (2009) "Phosphorylation of Ser205 by Casein kinase II persists on Pax3-FOXO1a, but not Pax3, throughout myogenic differentiation" *Biochemistry* 48:11786-11795. (PMCID: PMC2790557)
8. Dietz, K. N., Miller, P. J., Iyengar, A. S., Loupe, J. M., and **Hollenbach A. D.** (2011) "Identification of serines 201 and 209 as sites of Pax3 phosphorylation and the altered phosphorylation status of Pax3-FOXO1 during early myogenic differentiation" *Int. J. Biochem. and Cell Biol.* 43(6), 936 – 45. (PMCID: PMC3095663)

Additional publications (in chronological order):

9. **Hollenbach, A. D.**, McPherson, C. J., Mientjes, E. J., Iyengar, R. and Grosveld, G. (2002) "Daxx and histone deacetylase II associate with chromatin through an interaction with core histones and the chromatin-associated protein Dek" *J. Cell Sci.* 115, 3319-3330. (PMID: 12140263)
10. Sidhu, A., Miller, P. J., Johanson, K. E., and **Hollenbach, A. D.** (2008) Novel flanking DNA sequences enhance FOXO1a DNA binding affinity but do not alter DNA bending. *Biochemistry* 47:6809-18. (PMID: 18537265)
11. Bakkar, N., Wang, J., Ledner, K. J., Wang, H., Dahlman, J., Carathers, M., Acharyya, S., Rudnicki, M. A., **Hollenbach, A. D.**, and Guttridge, D. C. (2008) "IKK/NF- κ B Regulates Skeletal Myogenesis Via a Signaling Switch to Inhibit Differentiation and Promote Mitochondrial Biogenesis" *J. Cell Biol.* 180(4), 787 – 802. (PMCID: PMC2265568)
12. Sidhu, A., Miller, P.J., and **Hollenbach, A.D.** (2010) "Isolation of putative FOXO1 genomic elements using an improved in vitro technique to isolate genomic regulatory sequences." *Gene* 458(1-2): 45-5. (PMCID: PMC3126678)
13. Sidhu, A., Miller, P. J., and **Hollenbach, A. D.** (2011) "FOXO1 stimulates ceruloplasmin promoter activity in human hepatoma cells treated with IL-6." *Biochem. Biophys. Res. Commun.* 404: 963-7. (PMID: 21185807)
14. Abdraboh, M. E., Gaur, R. L, **Hollenbach, A. D.**, Sandquist, D., Raj, M. H. G., and Ouhthit, A. (2011) "Survivin, a novel target of CD44-promoted breast tumor invasion" *Am. J. of Pathol.* 179: 555 – 63 (June 14, epub ahead of print). (PMCID: PMC3157217)
15. Abdraboh, M. E., Errami, Y., Ouhthit, A., **Hollenbach, A. D.***, and Raj, M. H. G.* (2011) "The molecular interplay between the cell adhesion molecules CD44 and CD146 in breast cancer metastasis" *Cancer Res.* (manuscript submitted).

NOTE: asterisk (*) indicates these authors contributed equally to the manuscript

Patents:

1. Patent #7932030 – **Hollenbach, A. D.** and Johanson, K. E. "System for Pulling Out Regulatory Elements Using Yeast"
2. Patent Pending – **Hollenbach, A. D.** and Sidhu, A., "System for Pulling Out Regulatory Elements *in vitro*" (Application #11697154)
3. Patent Pending – **Hollenbach, A. D.**, Miller, P. J., and Dietz, K. N., "Phospho-specific anti-Pax3 Antibodies (Application #12477541)

D. RESEARCH SUPPORT:

Ongoing Research Support:

R01CA138656 Hollenbach (PI) 6/01/09 – 3/31/14
 NCI

"Mechanism of regulation for the oncogenic Pax3-FOXO1 in Alveolar Rhabdomyosarcoma"

This study, which is the originally funded R01 proposal, investigates how phosphorylation regulates the biological activities of the myogenic transcription factor Pax3, identifies the kinases that perform these phosphorylation events, analyzes how the oncogenic fusion protein Pax3-FOXO1 present in

Alveolar Rhabdomyosarcoma (ARMS) alters this normal regulation, and characterizes how phosphorylation contributes to the known ARMS phenotypes.

Role: PI

Research Support Completed During the Last Three Years:

P20 RR020152 Deininger/Keats (co-PIs) 9/01/04 – 5/31/09

NIH/COBRE

“The role of phosphorylation in the promotion of the solid muscle tumor Alveolar Rhabdomyosarcoma”

This was a mentored program grant intended to provide support for junior investigators to enable them to secure individual federal funding. The major goals of my individual project were to identify the sites of phosphorylation on the myogenic transcription factor Pax3, to determine how phosphorylation regulates the biological activities of Pax3, and to analyze how the oncogenic fusion protein Pax3-FOXO1 present in the childhood solid muscle tumor ARMS alters this normal regulation.

Role: Individual Project PI

The Louisiana Cancer Research Consortium, Competitive Advantage Fund

Hollenbach (PI) 9/1/07 – 10/31/08

“Identifying direct transcriptional targets important in the development of cancer”

The major goal of this project was to develop novel techniques for the isolation of genomic regulatory elements that are specifically bound by a known transcription factor and to analyze how mutated factors present in cancer alter this binding and regulation.

Role: PI